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THE MINUTE STRUCTURE OF THE GRAY NERVE-TISSUE.

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I N the year 18731 I made the following statements with regard to the structure-elements of the nervous system: Thin sections from the cortex or the main ganglia of a recently killed grown rabbit are the best specimens for examination with high powers of the micro-The section may be transferred to the slide with or without the addition of a preserving fluid; in the former instance a very dilute solution of bichromate of potash is preferable, because, as proved by A. Rollet, this does not alter the structure of protoplasm. Layers of protoplasm, with numerous formations like nuclei, ganglion-corpuscles of varying shapes, and medullated nerve-fibres of different sizes are seen. The living matter in the formations termed nucleoli, being compactly accumulated, is homogeneous and has a yellowish lustre; while in the protoplasma of all structure-elements of the nervous system the living matter is distributed in thin layers in the shape of granules and lumps, and is of an opaque gray color. All granules and lumps of the living matter are interconnected by means of delicate radiating spokes.

¹ Untersuchungen über das Protoplasma. Sitzungsber. d. Akad. d. Wissens in Wien.

In that article I first announced that all constituent elements of the gray nerve-tissue are constructed like protoplasm in general, viz., of a reticulum of living matter, the meshes of which contain a lifeless nitrogenous liquid. My illustrations plainly show this reticulum, both in the scattered nuclei, in the ganglionic corpuscles, and in the gray substance at large, the reticulum of the latter being uninterruptedly connected with that of the former.

The first observer, who maintained the presence of a delicate reticulum throughout the gray substance, more especially that of the spinal cord, was Gerlach, in 1870.2 Since he was able to trace the filaments of this reticulum to the ganglion-cells, nay, their direct transition into the bodies of these corpuscles, he, apparently, was right in claiming that the reticulum itself was nerve-tissue. This assertion. however, was contradictory to the well-established doctrine in physiology that all nerve-conduction is insulated. How could there be any insulation of nerve-impulses, if these were to run through a nervous network pervading the gray substance as a whole? While Gerlach's observation was admitted to be correct, his claim of the nervous nature of the delicate network has been doubted and overthrown by many excellent observers. Golgi, in 1873' and 1886,4 asserted that he was able to trace the filaments of the network to the ganglionic as well as to the connective tissue or glia-corpuscles, and, consequently, admitted the correctness of Gerlach's hypothesis in its essential features. At the same time he endeavors to draw a distinction between a purely nervous and a purely connective-tissue reticulum, denying the nervous nature of the broad or Deiters' offshoots.

S. Stricker, in 1883, thoroughly discusses the nature of the reticulum under question, pointing also to the broad offshoots of the ganglion-corpuscles, which were discovered by O. Deiters (1865), and termed by him "protoplasmic

² Art. Rückenmark. Stricker's Handbuch d. Lehre von den Geweben.

³ Tulla struttura d. sostan. grigia. Communic. prev. Milano.

⁴ Tulla fina anatomia degli org. centrali d. sistema nervoso. Milano.

⁵ Vorlesungen über allg. u. exper. Pathologie. Wien.

offshoots," the nature of which has remained entirely unsettled, since they could not be proved to become nerves, or axis-cylinders proper. Have we any right, Stricker argues, to call offshoots nervous, simply because they are in union

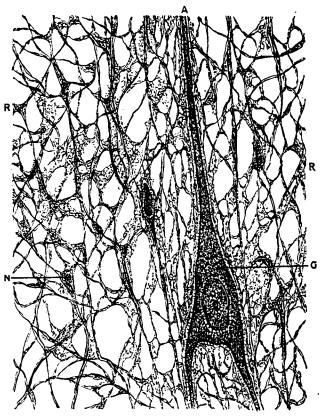


Fig. I.—Gray Nerve-tissue of the Spinal Cord of a Rabbit. Magn. = 1200. G Tripolar ganglionic corpuscle. A Axis-cylinder offshoot. R R Reticulum of living matter. N Neucleus forming point of intersection in the reticulum.

with ganglion-corpuscles? A similar reticulum exists in the outermost layer of the cortex of the brain, which lacks ganglion-corpuscles altogether, whose nervous nature had already been doubted by Meynert, and which nevertheless is continuous with the network of the deeper layers, so profusely supplied with ganglion-corpuscles. According

to Stricker, the meshes of the network are filled with a finely granular substance, rendered conspicuous by certain reagents to such an extent that the reticulum itself becomes concealed by it. This filling may furnish the gray substance with its peculiar consistency. Stricker considers the whole gray substance as inert, kindred to connective tissue, and considers nerve-action as existing only in the ganglion-corpuscles.

A. Forel,⁶ while admitting the correctness of Golgi's assertions, disagrees with this observer in regard to the central sensitive corpuscles. He says that all the sensitive nerves terminate in the reticulum of the gray substance without special centres. Kölliker (1887) is opposed to the assertion of Golgi, that the protoplasmic offshoots of the ganglion-corpuscles are not nervous in nature.

I have thus briefly given the most important literature on this topic in order to show that the minds of histologists are still unsettled concerning the nature of the reticulum, which so profusely traverses and builds up the gray substance. Not only do some observers deny it all activity, but Kühne and Ewald (1877) have even demonstrated a good deal of the reticulum to be keratoid, horny, not being digestible in pepsin and trypsin.

Fig. 1 gives an accurate representation of the morphology of the reticulum. The drawing is made from a specimen of the spinal cord of a rabbit, which was treated with osmic acid, cut with the microtome, and then stained with alumcarmine. We see that the reticulum in some portions is extremely minute, scarcely discernible with the excellent immersion-lens of Tolles, at my disposal, while in other portions it encloses somewhat larger meshes, which, to a certain extent, may have been produced artificially by the cutting and mounting procedures. The reticulum is continuous with that of the ganglionic corpuscle and that of the axis-cylinders. We can trace it to the walls of the capillary blood-vessels, where it traverses the narrow, peri-

⁶ Einige hirnanatom. Betrachtungen u. Ergebnisse. Arch. f. Psychiatrie, 1889.

vascular space, the same as it traverses the periganglionic space.

According to my views the gray substance is constructed in the same manner as protoplasm in general, i. e., by a reticulum of living or contractile matter and a liquid filling the meshes of the reticulum. The structure of the gray substance is identical with that of the ganglionic corpuscles and the scattered, apparently isolated nuclei: the only difference being that in the gray substance the reticulum of the living matter is extremely thin and delicate; in the central form-elements, on the contrary, comparatively coarse and dense. Besides, there may be a difference in the chemical constitution of the filling liquid, which difference, however, is not perceptible to the microscopist. have neither any right to call the reticulum nervous, in the sense of Gerlach, nor inert or connective tissue, as claimed by other authors.

In looking over the main varieties of connective tissue, i. e., the myxomatous, the fibrous, the cartilaginous, and the bony, we find as the most characteristic feature the so-This is greatly at variance in its called basis-substance. chemical constitution, even in apparently kindred forms of connective tissue. In one essential point, however, it is alike in all forms, viz., in filling the meshes of the reticulum and rendering it more or less consistent. The reticulum is concealed by the basis substance, and even in the myxomatous tissue never as plain as it appears in the gray nervetissue. It may be rendered conspicuous by different reagents, such as absolute alcohol, osmic acid, chloride of gold, etc. In the gray nerve-tissue such a basis-substance, the most important feature of connective tissue, is present only at the boundary-zone between the white and the gray substance (see Fig. 2, g), and in scanty bundles of a delicate fibrous connective tissue, which penetrate the gray from the white substance and run a radiating course through the former. At the boundary-zone the broad bundles of the interstitial inner perineurium rapidly decrease in bulk, for a short distance retaining a striated or fibrous structure, and soon splitting up into fibres which assist in building up the

reticulum. As long as the striated structure of bundles is recognizable, we have no reason to doubt the connective-tissue nature of the network. As soon, however, as the basis-substance proper is lost, the reticulum of living matter, traversing the basis-substance, is freed. Single granular fibrillæ, ever so conspicuously arising from the trabeculæ of the perineurium, are certainly not entitled to the name of connective tissue. Some of them may have undergone peculiar chemical changes (according to Kühne and Ewald, keratoid or horny), and thus serve as a supporting apparatus for the delicate reticulum; but they have ceased to be connective tissue. Where one ends and the other begins, the morphologist will never be able to tell.

Scanty bundles of fibrous connective tissue emanate from the pia-mater offshoots, which are likewise instrumental in constructing the inner prineurium and traverse the gray substance, as before mentioned, in a radiating direction. Probably they inosculate with the connective-tissue layer surrounding the ciliated epithelia of the central canal, although from personal observation I am unable to make such a statement positively. These bundles, being pierced by a reticulum of living matter, as all varieties of connective tissue are, profusely connect with the reticulum of the gray tissue, and again we are at a loss to tell at which point the basis-substance ceases and the living network has become free.

Unless chemical micro-reagents will be found, far more delicate than are at our disposal at the present time, I consider the task, to accurately discriminate in the gray nervetissue between fibrous connective tissue and fibrillæ of living matter, a hopeless one. What Stricker has claimed to be a granular filling mass is nothing but the most delicate portion of the reticulum itself, as evinced by the study of thin slabs with good immersion-lenses.

The reticulum, certainly in its main bulk, is alive during the life of the organism, and by its contractions causes that which we call nervous impulse. The reticulum of the gray substance is able to conduct in essentially the same manner, as that of the ganglionic corpuscles, by contraction, which

means narrowing of the reticulum and expansion, viz., widening of the reticulum. The effect will, however, be different in the widespread, loosely arranged, and extremely delicate network of the gray tissue and the dense, compact one of the ganglionic corpuscles. Both being identical in their nature, the final result may depend merely on the anatomical differences in the distribution and compactness. Any living lump of protoplasm is, as is acknowledged to day, movable and sensitive without a trace of nerves. amæba creeps and evades obstacles in its way, it perceives the light, though it is built up by nothing but a reticulum of living matter, without differentiation into nerves or nervecentres. Looking at the structure of the gray substance in this light, all difficulties in explaining its histological nature will fade away, and nerve-action becomes explicable. The absolute insulation of nerve-impulse is, consequently, done away with, and numerous physiological and pathological observations strongly point toward the absence of a perfect insulation within the nerve-centres.

The second topic under consideration is the structure of the axis-cylinder. This term includes the non-medullated nerve-fibres as well as the initial portions of the medullated nerve-fibres as yet destitute of a medullary investment.

Max Schultze, in 1868, was the first to assert that the axis-cylinders have, in many instances, a fibrillated structure which he claimed to be continuous with the fibrillated structure within the ganglionic corpuscles. S. Stricker, in 1883, admits that he saw the convincing specimens of Max Schultze, but at the same time declares that he was never able to see the fibrillated structure of the axis-cylinders in specimens of brains that were brought into hardening liquids immediately after the death of the animal. What the structure of the axis-cylinder is, this author does not say. I made the following statement in 1883: "With high am-

⁷ Die Structurelemente des Nervensystems. Handbuch d. Lehre von den Geweben, von S. Stricker.

⁸ Vorlesungen über allg. u. exper. Pathologie, p. 576.

⁹ Microscopical Morphology, p. 298. New York.

plifications of the microscope, some of the larger nonmedullated nerve-fibres distinctly show a delicate reticular structure; others exhibit a number of minute vacuoles in their interior; still others, and these are the finest nervefibres, have a homogeneous appearance and give no evidence of structure." On page 300 I publish a diagram of nerve-conduction, in which the axis-cylinders, as well as the ganglionic corpuscles themselves, are drawn reticular throughout. Should A. Forel's above-quoted views be correct, the presence of a sensitive nerve-ganglion will prove to be a fallacy, but would have to be replaced by a reticulum of living matter within the gray substance, into which also the broad or Deiters' offshoot ought to inoscu-That much plainly follows from my diagram, that I consider the structure of the axis-cylinder identical with that of the ganglionic corpuscles, viz., made up of a reticulum of living or contractile matter, much more delicate and dense in the axis-cylinders than in the ganglionic cor-In the latter elements this structure is scarcely a subject of doubt, and since it was first discovered by C. Frommann (in 1867) has oftentimes been described and illustrated by excellent histologists; whereas the reticular structure of the axis-cylinder, at least as far as I know, was corroborated only quite recently by Max Joseph (1888).10 This observer has investigated the electric nerve-fibres of torpedo marm. He denies the keratoid or horny nature of the network within the myelin investment of the medullated nerves, since, contrary to the claim of Kühne-Ewald, it is dissolved by pepsin and trypsin, and demonstrates the presence of a much more delicate network in the axiscylinder.

The question now arises: How was it possible that Max Schultze, one of our most skilled observers in microscopy, could have seen a fibrillated structure in the axis-cylinders? For nobody will doubt that such a structure was visible, if so asserted by M. Schultze. There is but one explanation to this strange fact, viz., the faulty method of teasing nerve-

¹⁰ Berliner Akademie-Bericht, p. 1321. Quoted from Edw. Klebs, Allg Pathologie, II. Theil, 1889.

specimens and their mounting in Canada balsam. We can realize that by dragging delicate structures, such as those of ganglion-corpuscles and axis-cylinders are, the reticulum will be drawn out and be artificially transformed into a series of fibrillæ. At first teasing was done by M. Schultze in an indifferent liquid, the iodine-serum, and afterward, for fixation, alcohol and osmic-acid solution were resorted to. Fortunately, nowadays, all mutilating methods, such as

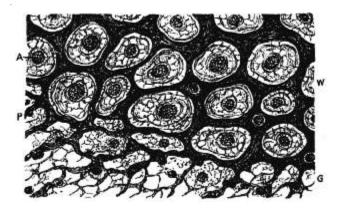


Fig. II.—Boundary zone between the Gray and White Nerve-Tissue. Spinal Cord of a Rabbit. Transverse section. Magn. = 1200. G Gray nerve-tissue. W White nerve-tissue. A Axis cylinder. P Perineurium.

tearing and teasing unquestionably are, have fallen into discredit, and find application only by narrow-minded histologists, who are unable to appreciate the sad consequences of mechanical injuries and of laceration of tissues, the structure of which becomes comprehensible only by a strict conservation of integrity and continuity.

Since 1873 I have been convinced of the reticular structure of all nerve-elements to such an extent that I considered the ultimate axis-fibrillæ—composed of granules and a single inter-connecting thread, rendering these fibres rosary-like—merely a linear projection of the reticulum, inosculating with the living matter, both at the periphery and in the central gray tissue. To-day I have no reason to change my views, after having studied a number of specimens,

treated with widely different methods. Fig. 1 shows the delicate reticular structure in the axis-cylinder running longitudinally; Fig. 2, the transverse sections of these formations within the white mantel of the spinal cord.

Fig. 2 represents the boundary-zone between the white and gray substance, in the transverse section of the spinal cord of a rabbit. The specimen was treated first with osmic acid and afterward with alum-carmine solution. It is striking that the osmic acid did not stain the myeline in a darkbrown color, but the interstitial inner perineurium, the transition of which into the reticulum of the gray tissue is well shown. The axis-cylinders plainly exhibit a finely reticular structure. Around them we recognize a delicate sheath, the axis-cylinder sheath of L. Mauthner, and at the periphery of the fibre the sheath of Schwann, enclosing the myeline. Besides, here and there are visible other concentrically arranged layers, the significance of which I am unable to tell. The space, previously occupied by the myeline, is traversed by a knotty, irregular network, first described by Kühne and Ewald in 1886," and claimed to be keratoid or horny by these observers, owing to the fact that it remains undigested under the influence of pepsin and trypsin.

In the finest axis-cylinders I am unable to discover any structure whatever, which does not exclude the possibility of a structure becoming recognizable, at some future time, by improved optical or staining appliances.

The presence of a contractile reticulum within the axiscylinder would enable us to endeavor reducing nervous action to contractility, a feature found in all protoplasmic formations. The denser and more delicate the reticulum of living matter, the more rapid will be its contraction, furnishing the physiological basis of all nervous impulse. Centripetal contraction will be felt as sensation; centrifugal will result in motion. The nerves, when viewed in this light, merely convey rapid contractions. They may be considered as an apparatus of refinement of physiological

¹¹ Verhandl. d. Heidelberger Gesellsch.

properties, common to every living lump of protoplasm, animal as well as vegetable, i. e., sensation and motion.

The third and last topic of my paper is the origin of axis-cylinders, or nerve-fibres, from the reticulum of the gray substance.

O. Deiters, in 1865,12 made the assertion that from a ganglionic corpuscle, the number of its offshoots being ever so large, probably but one offshoot arises which is a true axis-cylinder, and which, coursing toward the periphery, respectively the white substance of the brain and spinal cord, becomes a nerve proper. Since that time this fact is generally admitted as correct. Deiters called all the other offshoots protoplasmic or branching. J. Gerlach, the discoverer of the nervous reticulum in the gray substance, in 187013 first made the statement that Deiters' offshoots inosculate with the nerve-reticulum, and true axis-cylinders originate from this reticulum, not being in direct union with any ganglionic corpuscle. His description of the method best suited for the demonstration of this fact is briefly as follows: "A perfectly fresh, yet warm spinal cord of a calf or ox is sliced with the razor into very thin longitudinal sections, best through the anterior horns, and immediately placed into a very dilute solution of bichromate of ammonia (I to 5,000 or 10,000 water) for two or three days. this the slabs are placed into dilute ammoniacal carmine, and, after twenty-four hours, are torn up by means of needles, with special care for the preservation of the darkred nerve-cells. Such specimens are preserved in glycerin, or, preferably, allowed to dry, and, after addition of a minute quantity of oil of cloves, mounted in Canada balsam."

I have purposely quoted Gerlach's words, in order to show that his assertions were based upon the study of teased specimens, as is also illustrated by his Fig. 223, the object of which is to demonstrate the origin of a branching nerve-fibre from the nerve-reticulum. No wonder,

¹² Untersuchungen über Gehirn u. Rückenmark.

¹³ Art. Rückenmark. Handbuch der Lehre von den Geweben, von S. Stricker.

therefore, that but little attention was paid to Gerlach's statement, which, nevertheless, is perfectly true.

In my "Microscopical Morphology" (1883), on page 288, I quote Gerlach's discovery, as follows: "The offshoots of the ganglionic elements are of two kinds: the broad, so-called protoplasmic offshoots of Deiters, and the narrow,

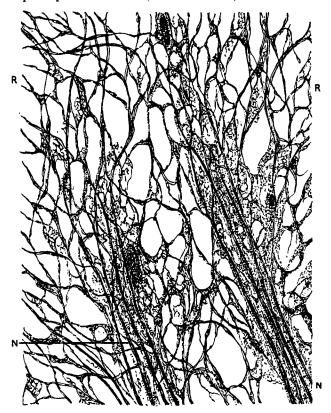


Fig. III.—Origin of Nerve-Fibres from the reticulum of living matter. Gray Nerve-tissue of the Spinal Cord of a Rabbit. Magn. = 1200. NN Bundles of nerve-fibres. RR Reticulum of living matter.

axis-cylinder offshoots. Of the former we know that they connect neighboring elements, and branch out into the gray substance, where they divide into an extremely delicate reticulum, first described by J. Gerlach. This author further asserts that the ganglionic elements of Clarke's columns,

and perhaps those of the posterior horns also, have no other than branching offshoots." On page 290: "According to Gerlach, it is also probable that from the reticulum of the posterior horn nerve-fibres originate, which in this horn and in the white substance take a centripetal course." On page 288 I make the following assertion, independently of Gerlach and based upon observation of sections of the spinal cord, carefully preserved in their continuity: "Axis-cylinder offshoots arise also from the gray substance, without any connection with ganglionic elements." This statement is a corroboration of that of Gerlach.

In order to show how such a statement could be made from the study of a sliced specimen, I affix Fig. 3, obtained from a spinal cord first treated with a one-per-cent. osmicacid solution and afterward with alum-carmine.

We see the reticulum—the region is that of the anterior commissure branching into the gray tissue of the anterior horn—condensed into filaments, which, gradually assuming an increasing diameter, are traceable a great distance into the gray tissue, and have no other connections with the adjacent reticulum but the delicate lateral spokes visible on axis-cylinders generally, including those that plainly arise from a ganglionic corpuscle. Can there be any doubt as to the nervous nature of such filaments? I should think not.

In the posterior horns there are no ganglionic corpuscles proper; only formations like nuclei, which, in my conviction, serve as central formations, since in the brain of the lowest vertebrates they are the only elements visible in the gray tissue. My teacher, E. Brücke, often asserted that nobody has as yet been able to see nerve-fibres emanate from such nuclei in the posterior horns, and Gerlach's statement, that all sensitive nerves of the posterior horn inosculate with the reticulum of the gray tissue, is certainly correct. In 1883, while in Paris, L. Ranvier, the ablest French histologist, was kind enough to show me what he considered glia-cells, therefore connective-tissue elements, freely branching into innumerable offshoots and producing around the "cell" a delicate network. Golgi (loc. cit.) made at-

tempts to discriminate between a nervous and a connectivetissue reticulum, but failed to convince the histologists, since the differences in the taking up of certain coloring matters are altogether too slight. What an embarrassment, if the whole reticulum should be connective tissue, or horny material inert! Deiters' offshoots branch into it and axiscylinders arise from it. Where are we to locate the centres of the sensitive nerves, if these inosculate with a connectivetissue reticulum?

There is but one way to escape all these difficulties, and this is to consider the reticulum as neither nervous nor connective tissue, but living or contractile matter. With this view an indirect connection is established between all central elements of the gray tissue, the nuclei, and the ganglionic corpuscles; though, I admit, the theory of a perfect insulation is lost. Similar formations we meet with in the retina, and there is no end of quarrels as to the nervous or connective-tissue nature of a number of filaments and reticular formations. Here, too, all difficulties could be overcome by simply admitting that the reticulum is living or contractile matter.

Quite recently an important confirmation of Gerlach's original assertion has been made by Béla Haller (1886). This author demonstrated, in the ganglia of molluscs, marginal ganglionic corpuscles and a reticulum emanating from them. Some of the offshoots of the latter directly become nerve-fibres, whereas the majority of the nerve-fibres originate from the reticulum. Thus we are positive of a double origin of nerve-fibres. L. Edinger is thoroughly convinced of this view, and we have good reasons to accept an excellent observer's coincidence with facts so much in harmony with the most advanced modern biological views.

More and more we approach the doctrine, first established by myself in 1873, which claims that the living matter is continuous throughout the whole animal organism. The

¹⁴ Untersuchungen über marine Rhipidoglossen: II. Textur des Centralnervensystems. Morphol. Jahrb., XI.

¹⁵ Schmidt's Jahrbücher, Jahrgang 1887, No. 8.

apparently well-founded cell-theory must be sacrificed in order to obtain a plain understanding, not only of the action of nerve-tissue, but of the whole organism. The nerve-tissue is long since acknowledged to be continuous throughout the body: it will take but one step further to establish the continuity and life of all tissues constituting the animal and vegetable body.

In the United States the progress of the novel views, which are not the worse for being dubbed by the late L. Elsberg the "bioplasson-theory," is slow but steady. Charles F. Cox, in an excellent presidential address, delivered before the New York Microscopical Society, on January 3, 1890, expresses this progress in the following manner:

"I can well remember, as perhaps you also can, the disgusted incredulity with which this new doctrine was received—an incredulity in which, I confess, I then shared. I am not sure that the appearance of a reticulum in the prepared blood-corpuscle is even yet generally accepted as evidence of a normal structure of the kind claimed by Dr. Heitzmann; but the claim certainly gains support from the fact that vegetable histologists are pretty well agreed that a more or less similar reticulum is demonstrable in the protoplasm of plants. Prof. Goodale seems to have no doubt on this point.

"In the work from which I have just quoted, "Dr. Heitzmann generalizes as follows: 'What... was called a structureless, elementary organism, a "cell," I have demonstrated to consist only in part of living matter, while even the minutest granules of this matter are endowed with manifestations of life. The cell of the authors, therefore, is not an elementary, but a rather complicated, organism, of which small detached portions will exhibit amæboid motions.... How complicated the structure of a minute particle of living matter may be, we can hardly imagine; what we do know is that the so-called "cell" is composed of innumerable particles of living matter, every one of which is endowed with properties formerly attributed to the cell-organism."

¹⁶ Microscopical Morphology. New York, 1883.

"It having been shown that life hangs upon a web of infinite tenuity, and does not reside necessarily in either a vesicle or a lump, it was a natural and easy step to extend this network from tissue to tissue and organ to organ, in an unbroken circuit of vital communication. This step Dr. Heitzmann does not hesitate to take; for, says he, 'there is no such thing as an isolated, individual cell in the tissues, as all cells prove to be joined throughout the organism, thus rendering the body in toto an individual. What was formerly thought to be a cell, is, in the present view, a node of a reticulum traversing the tissue. . . . The living matter of the tissues exists mainly in the reticular stage, and is inter-connected without interruption throughout the body.'

"Again, this at first very strange and, for some reason or another, unwelcome doctrine receives support from the investigations of botanists; for, as Prof. Goodale remarks, this protoplasmic inter-communication between adjoining cells 'has been shown to be so widely true in the case of the plants hitherto investigated, that the generalization has been ventured on that all the protoplasm throughout the plant is continuous.' The position to which we have traced this matter is, then, that to the latest biology, in any particular organism, a generally diffused and inter-connected substance, simple only in appearance under present optical aids, has taken place of the circumscribed, more or less isolated and independent, and recognizably complex vesicle which was the physical basis of life to the science of fifty vears ago. In the words of Dr. Heitzmann: 'According to the former view, the body is composed of colonies of amæbæ; according to the latter, the body is composed of one complex amœba.'"

Truth is welcome, from whatever quarters it may come. In the support of the recent views the botanists have proved to be superior to animal biologists. Still, the plants have no central nerve-organs, no nerves. How much plainer is the truth evinced by an unbiased study of the structure of the gray nerve-tissue!